

Qualified requesters may obtain copies of this report from DDC. Orders will be expedited if placed through the librarian or other person designated to request documents from DDC.

When U. S. Government drawings, specifications, or other data are used for any purpose other than a definitely related government procurement operation, the government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

This document has been approved for public release and sale; its distribution is unlimited.

DDC	
CFSTI	WHITE SECTION <input checked="" type="checkbox"/>
ROC	DIFF SECTION <input type="checkbox"/>
IF ANNOUNCED	
JUSTIFICATION	
BY	
DISTR BU "10" AVAILABILITY CODE	
DIST.	AVAIL. AND/OR SPECIAL

UNCLASSIFIED

AD 666 647

EFFECT OF P_{CO_2} ON THE RELATION OF LACTATE AND
EXCESS LACTATE TO O_2 DEFICIT

Stephen M. Cain

School of Aerospace Medicine
Brooks AFB, Texas

December 1967

Processed for . . .

DEFENSE DOCUMENTATION CENTER
DEFENSE SUPPLY AGENCY



U. S. DEPARTMENT OF COMMERCE / NATIONAL BUREAU OF STANDARDS / INSTITUTE FOR APPLIED TECHNOLOGY

UNCLASSIFIED

EFFECT OF P_{CO_2} ON THE RELATION OF LACTATE AND EXCESS LACTATE TO O_2 DEFICIT

STEPHEN M. CAIN, Ph.D.

FOREWORD

This report was prepared in the Physiology Branch under task No. 775801. The work was accomplished between December 1966 and September 1967. The paper was submitted for publication on 18 September 1967.

The animals involved in this study were maintained in accordance with the "Guide for Laboratory Animal Facilities and Care" as published by the National Academy of Sciences—National Research Council.

The author is grateful for the technical assistance of Mrs. M. Kardon, A. Sanchez, and W. Soucie, and for the statistical analyses and advice supplied by Dr. Phelps P. Crump.

This report has been reviewed and is approved.



GEORGE E. SCHAFER
Colonel, USAF LSC
Commander

ABSTRACT

When anesthetized dogs were made hypoxic at constant ventilation, increases in arterial lactate (ΔL) compared as well to net O_2 deficit (NOD) as did excess lactate (XL). It was asked whether this would hold true if PCO_2 was varied during hypoxia. Twelve dogs were made hypoxic for 30 minutes while eucapnic ($PCO_2 = 40$ torr) and again while hypercapnic ($PCO_2 = 77$ torr), with appropriate control and recovery periods. Another group of 12 dogs were treated similarly except one hypoxic period was hypocapnic ($PCO_2 = 18$ torr) and the other eucapnic. NOD was estimated from the total decrease in $\dot{V}O_2$ during hypoxia by assuming that baseline $\dot{V}O_2$ would have been unchanged if PO_2 was not limited, and by estimating the change in O_2 stores during hypoxia. Net O_2 repayment (NOR) was estimated similarly. In a graph of ΔL against NOD three different lines were obtained according to the PCO_2 level. The same was true for XL against NOD. In 36 of 48 comparisons, NOR was less than NOD. Of the 12 comparisons in which NOR was larger, 7 were hypocapnic, 4 were eucapnic, and only 1 was hypercapnic. In addition to direct effects of altered intracellular pH on lactate metabolism, PCO_2 may also alter baseline energy demand during hypoxia by its effect on calorogenesis of liberated catecholamines.

EFFECT OF P_{CO_2} ON THE RELATION OF LACTATE AND EXCESS LACTATE TO O_2 DEFICIT

I. INTRODUCTION

When the increases in arterial lactate and excess lactate were compared to the oxygen deficit incurred during hypoxic exposures of anesthetized dogs, the lactate increase correlated better than did the peak excess lactate (2). Because ventilation was maintained nearly constant in those experiments, hypocapnia, which usually accompanies hypoxia, did not develop. It was suggested that the superimposed effect of hypocapnia, which increases blood lactate, on that of hypoxia would have decreased the high correlation of lactate increase (ΔL) with oxygen deficit. Excess lactate (XL) was supposed to be independent of the hypocapnic effect (7). That hypothesis was tested in the experiments reported here. The results establish that the PCO_2 level during hypoxia indeed alters the lactate accumulation for a measured O_2 deficit and that excess lactate is not independent of this effect.

II. METHODS AND PROCEDURES

Two groups of 12 dogs each were used. All were anesthetized with sodium pentobarbital (30 mg./kg.) and were prepared and treated as described previously (2). Two hours elapsed after the animal was anesthetized before beginning the experiment. During that time, catheters were inserted in both femoral arteries and veins and the pulmonary artery, and a tracheal cannula was tied in place. After an initial 30 mg. intramuscular injection of succinylcholine chloride, 0.1 mg./min. in saline was infused continuously into the femoral vein. The tracheal cannula was connected to a Harvard respirator set so that end-tidal PCO_2 was approximately 40 torr. After a stabilization period, the experiment was begun.

The sequence for each animal was the same (table I): a 30-minute control period breathing air followed by 30 minutes of hypoxia, which was followed in turn by a 30-minute recovery period in air, and the entire cycle was then

TABLE I

Sampling schedule for O_2 uptake (gas sample), lactate and pyruvate (pipet sample), and gas tension, O_2 content, and pH of arterial and mixed venous blood (syringe samples)

Period	Gas sample	Pipet sample	Syringe sample
		Minutes	
Control I	0 - 10		
	10 - 20	15	
	20 - 30	30	28
Hypoxia I	30 - 40		
	40 - 50		
	50 - 60	60, 61, 62	58
Recovery I	60 - 70		
	70 - 80		
	80 - 90		88
Control II	90 - 100		
	100 - 110	105	
	110 - 120	120	118
Hypoxia II	120 - 130		
	130 - 140		
	140 - 150	150, 151, 152	148
Recovery II	150 - 160		
	160 - 170		
	170 - 180		
	180 - 190	190	
	190 - 200		
	200 - 210		178

repeated. This insured that hypoxic periods were separated by a full hour during the procedure. In group I, one hypoxic period was induced by allowing the dog to breathe 9.3% O₂ in N₂ while the respirator setting was not changed (eucapnia). The second hypoxic period in the same animal was induced either by severe hypoventilation achieved by reducing the respirator cycling rate or by leaving the setting unaltered and connecting a gas mixture of 9.5% O₂ and 7.2% CO₂ in N₂ (hypercapnia). Hypercapnic hypoxia was produced by hypoventilation in 6 of the 12 animals in group I. Analyses of results did not reveal any differences due to the method of producing hypercapnia. The order of presentation of eucapnic and hypercapnic hypoxia was alternated for each experiment.

The procedures for group II were the same except eucapnic hypoxia was alternated with hypocapnic hypoxia during which the respirator rate was increased and the animal breathed a lower O₂ mixture (4.9% to 5.1% O₂ in N₂). In both groups, expired gas was collected continuously in 10-minute samples and blood samples were taken according to the schedule shown in table I for analyses of lactate, pyruvate, blood gas tensions and contents, and pH. The analytical methods have been described (2).

To measure total O₂ deficit during hypoxia and the excess O₂ uptake during the recovery period, it was assumed that the control or baseline O₂ uptake would have prevailed unchanged during these periods if it had not been altered by the imposed experimental condition. Thus, the total O₂ deficit was the area enclosed by the extrapolated baseline O₂ uptake and the measured uptake. The excess O₂ uptake during the "repayment" or recovery period was obtained similarly. As reported previously (2), O₂ uptake was always decreased during hypoxic periods and increased during recovery periods before returning to the baseline level.

The total O₂ deficit and repayment included changes in O₂ stores which were depleted from control levels during hypoxia and replenished during recovery. To obtain net O₂ deficit

(NOD) and net O₂ repayment (NOR), changes in O₂ stores were estimated from the following relationships and subtracted from the total deficit and repayment.

$$\text{External dead space O}_2 \text{ (ml./kg.)} = (200 - F_{I\text{O}_2}) \left(\frac{530 + \frac{1}{2} \text{ S.V.}}{W} \right) \quad (1)$$

where S.V. is the stroke volume of the respirator and W is weight of the dog in kilograms. The volume of external dead space of tubing and the respirator (530 ml.) and the stroke volume are at standard conditions.

$$\text{Lung O}_2 \text{ stores (ml./kg.)} = \left[\frac{(P_{a\text{O}_2}) \text{ C or R} - (P_{a\text{O}_2}) \text{ H}}{P_{\text{B}} - P_{\text{H}_2\text{O}}} \right] \times 24 \quad (2)$$

where C is control, R is recovery, and H is hypoxia. The functional residual capacity of dogs was taken to be 24 ml./kg.

$$\text{Tissue water O}_2 \text{ stores (ml./kg.)} = \left[\frac{(P_{v\text{O}_2}) \text{ C or R} - (P_{v\text{O}_2}) \text{ H}}{760} \right] \times 600 \times .0214 \quad (3)$$

where .0214 is the Bunsen solubility coefficient for plasma at 38° C. and 600 ml./kg. represents body water fraction.

$$\text{Blood O}_2 \text{ stores (ml./kg.)} = \frac{1}{3} \left[\frac{(C_{a\text{O}_2}) \text{ C or R} - (C_{a\text{O}_2}) \text{ H}}{100} \times 90 \right] + \frac{2}{3} \left[\frac{(C_{v\text{O}_2}) \text{ C or R} - (C_{v\text{O}_2}) \text{ H}}{100} \times 90 \right] \quad (4)$$

where 90 represents milliliters of blood per kilograms of body weight, and it is assumed that one-third of the total blood volume is arterial in nature and the rest has the composition of mixed venous blood.

A discussion of the basis for selection of these factors and the probable error accruing from the several assumptions will be found in the earlier work (2).

III. RESULTS

Mean values of blood gas tensions, pH, and saturation, as well as rectal temperature and the oxygen uptakes used as baselines, are shown in table II. All the data from control periods

TABLE II

Summary of blood gas data, pH, rectal temperature, and control O₂ uptake

Period	Group I		Group II	
	Eucapnia	Hypercapnia	Eucapnia	Hypocapnia
P_aO₂ (mm. Hg)				
Control	83.3 ± 7.1*	82.1 ± 7.0	78.5 ± 6.4	78.7 ± 6.5
Hypoxia	19.0 ± 1.5	27.0 ± 8.9	18.3 ± 2.7	15.9 ± 1.8
Recovery	78.7 ± 8.5	80.6 ± 6.9	77.3 ± 9.6	75.6 ± 8.8
P_vO₂ (mm. Hg)				
Control	45.8 ± 3.4	45.4 ± 3.5	45.8 ± 3.0	43.2 ± 3.5
Hypoxia	11.7 ± 2.0	17.7 ± 7.6	10.4 ± 3.1	8.6 ± 2.7
Recovery	43.9 ± 3.6	46.1 ± 2.3	45.3 ± 2.5	43.8 ± 3.7
P_a-CO₂ (mm. Hg)				
Control	40.6 ± 2.9	38.4 ± 2.7	40.6 ± 5.6	40.9 ± 4.5
Hypoxia	39.4 ± 5.7	76.5 ± 8.5	42.9 ± 5.5	18.1 ± 1.9
Recovery	38.9 ± 3.7	43.5 ± 3.8	42.1 ± 7.4	38.2 ± 6.1
pH_a				
Control	7.349 ± .024	7.369 ± .029	7.327 ± .035	7.320 ± .045
Hypoxia	7.335 ± .047	7.114 ± .035	7.260 ± .061	7.457 ± .089
Recovery	7.343 ± .029	7.301 ± .021	7.273 ± .06	7.292 ± .071
S_aO₂ (%)				
Control	91.3 ± 2.7	91.2 ± 2.5	91.9 ± 3.2	91.5 ± 4.1
Hypoxia	20.0 ± 7.6	23.6 ± 15.3	23.8 ± 9.7	27.5 ± 4.0
Recovery	89.9 ± 3.3	89.5 ± 3.0	89.5 ± 6.8	89.3 ± 6.6
S_vO₂ (%)				
Control	71.3 ± 4.6	71.2 ± 5.6	71.9 ± 6.6	72.4 ± 7.5
Hypoxia	8.2 ± 5.3	13.0 ± 12.2	13.9 ± 8.6	14.0 ± 13.6
Recovery	67.0 ± 6.8	66.2 ± 5.4	68.1 ± 7.8	67.2 ± 9.8
T_r (° C.)				
Control	37.7 ± .7	37.7 ± .6	38.1 ± .7	38.0 ± .6
Hypoxia	37.5 ± .7	37.6 ± .7	37.8 ± .8	37.6 ± .6
Recovery	37.9 ± .8	37.9 ± .6	38.0 ± .9	38.0 ± .7
\dot{V}O₂ (ml./kg./min.)				
Control	6.45 ± .68	6.50 ± .64	6.43 ± .93	6.51 ± 1.06

*Mean ± S.D.

were comparable in that no significant differences were found. In general, the animals were well oxygenated during control and recovery periods, and initial arterial PCO₂ values were about 40 torr, as they were intended to be. Rectal temperature showed an insignificant tendency to decrease during hypoxic periods, but this was largely prevented by use of an electric heating pad. The average arterial PCO₂ during hypercapnic hypoxia was about 77 torr

and 18 torr during hypocapnic hypoxia so that the two conditions were well separated from the eucapnic hypoxic values of about 40 torr. The corresponding differences in pH were not quite as well marked, but differed significantly from the eucapnic values measured in the same groups. On the whole, the experimental design was satisfactory to distinguish three well-differentiated ranges of PCO₂ and pH during hypoxia periods.

Three distinct groups of points resulted when the relationship of the peak lactate increase over the control value (ΔL) and net O_2 deficit (NOD) was examined (fig. 1). The eucapnic hypoxic dogs of group I did not yield any different results from those of group II so the data were treated in common. The equation of the linear regression line fitted to these data was $\Delta L = 0.66 + 0.088 \text{ NOD}$, and the coefficient of correlation was .92. For the hypercapnic data, the equation was $\Delta L = 0.068 \text{ NOD} - 0.90$, and the correlation coefficient was .72. Regression analysis indicated that the slopes of these two lines did not differ significantly but that the intercepts did. The line

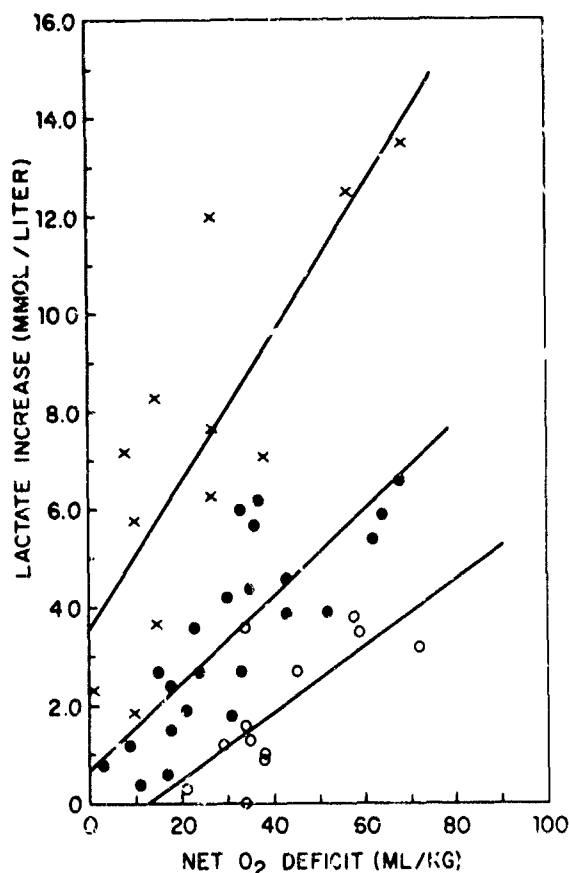


FIGURE 1

Peak lactate increase compared to net O_2 deficit incurred during hypoxia—hypercapnic, eucapnic, and hypocapnic.

Key: ○—Hypercapnic.
●—Eucapnic.
×—Hypocapnic.

fitted to the hypocapnic data, on the other hand, had a significantly different slope, the equation being $\Delta L = 3.54 + 0.15 \text{ NOD}$, with a correlation coefficient of .81.

When excess lactate was graphed against NOD (fig. 2), similar results were obtained. Eucapnic and hypercapnic data could be fitted by lines of the same slope but different intercept, whereas hypocapnic points fitted a line that differed in both. The separately calculated linear regressions and correlation coefficients were, respectively, for eucapnia, hypercapnia, and hypocapnia: $XL = 0.49 + 0.069 \text{ NOD}$, $r = .79$; $XL = 0.049 \text{ NOD} - 0.53$, $r = .64$; and $XL = 1.65 + 0.136 \text{ NOD}$, $r = .85$. With the exception of the hypocapnic data, excess lactate did not correlate as well with NOD as did the lactate increase. The correlation coefficients for the eucapnic data were almost the same as obtained in the first study (2).

Lactate increase and XL were also related to the net excess oxygen of recovery (net O_2 repayment, NOR). Figures 3 and 4 illustrate

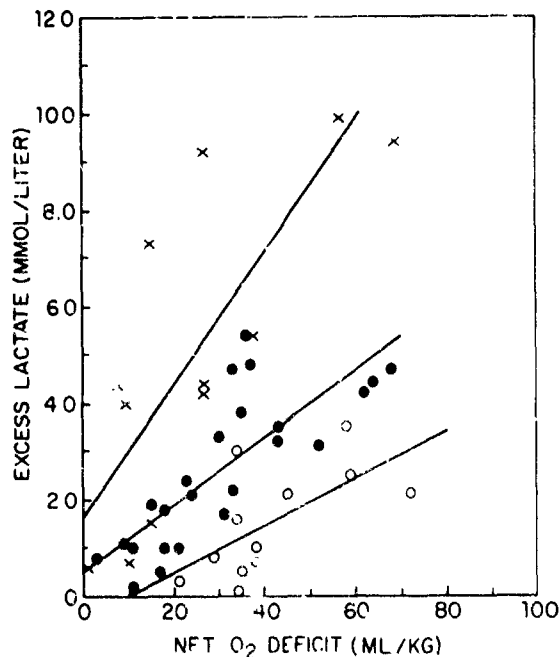


FIGURE 2

Peak excess lactate compared to net O_2 deficit incurred during hypoxia—hypercapnic, eucapnic, and hypocapnic.

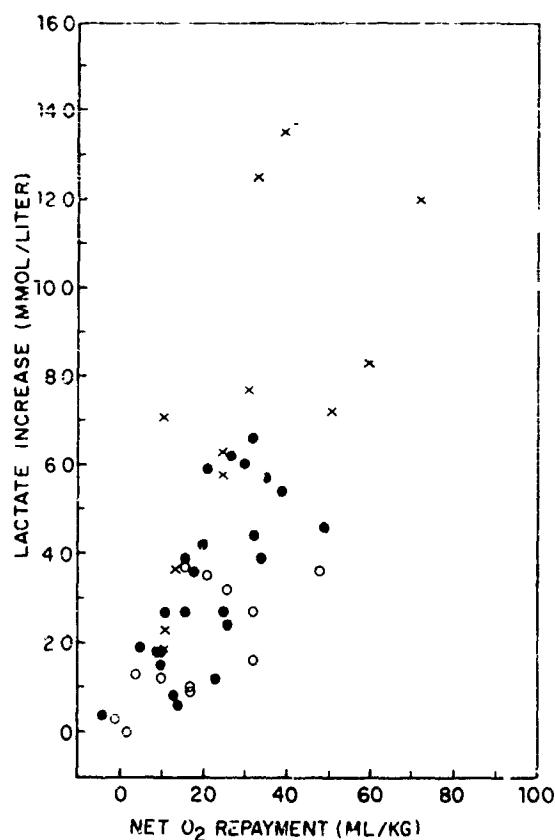


FIGURE 3

Peak lactate increase accumulated during hypoxia—hypercapnic, eucapnic, and hypocapnic—graphed against the net O_2 repayment after these periods.

that although there was a tendency toward grouping according to the CO_2 range, there was much more overlap between groups. Regression analysis indicated that the slope of the best fitting line for the hypocapnic data was not significantly different from the others but that the intercept was different and the eucapnic and hypercapnic points could be fitted as well by a single line as they could by separate lines. Because the PCO_2 condition of the hypoxic period was not maintained during the recovery period, only a partial or residual effect may have been evident in the recovery data.

A similar criticism holds for figure 5 in which NOR and NOD are compared. Some interesting differences are evident, however.

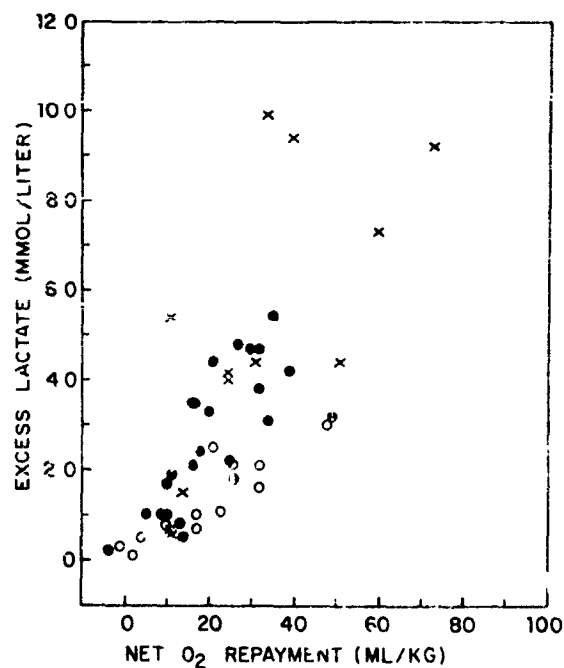


FIGURE 4

Peak excess lactate accumulated during hypoxia—hypercapnic, eucapnic, and hypocapnic—shown in relation to the net O_2 repayment.

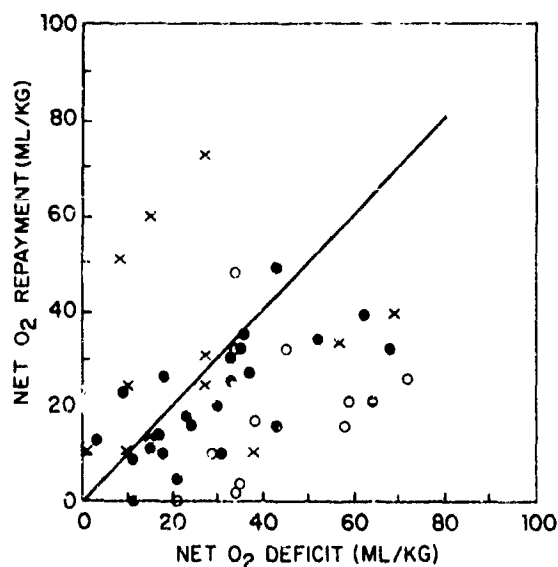


FIGURE 5

Net O_2 repayment is shown as a function of the net O_2 deficit incurred during hypoxia—hypercapnic, eucapnic, and hypocapnic. The line is drawn through equal values for both axes.

In the comparisons, NOR was less than NOI. In comparisons in which NOR was less than NOI, 4 were hypocapnic, 4 were eucapnic, and 4 were hypercapnic. The repayment of O_2 deficit was significantly more following hyperventilation than it was following eucapnic or hypercapnic hypoxia. Even between the latter groups there appears to be a tendency for less repayment in the high PCO_2 range, but the statistical analysis did not reveal any significant difference.

DISCUSSION

The net O_2 deficit, as measured in these experiments, is a valid index of the energy deficit caused by the hypoxic limitation of energy metabolism. Then the data force the conclusion that the complicated measurement of lactate serves no better than the measurement of net O_2 deficit as a measure of hypoxic energy deficit. It is supposed to be independent of PCO_2 effect. The reason for this requires extrapolation.

Hyperventilation alone increases lactate (5, 14) and for periods of one hour or less, causes little or no formation of excess lactate (7, 16). Although lactate increase has been thought to be solely the result of hypocapnia (4), there is ample reason to believe that intracellular pH is at least as important, if not the key factor (14). In fact, Katzman et al. (8) showed that incubated dog tissues produced more rather than less lactate with increasing CO_2 concentration if pH was held at 7.4, and failed to do so only when pH of the medium was lowered below 7.1. The effect of hypercapnia alone, on the other hand, is to depress lactate levels in the body (1, 9). This corresponds to the results obtained by Katzman et al. (8) from their in vitro system when bicarbonate concentration was held nearly constant. Thus, lactate changes in vivo appear to vary inversely with PCO_2 .

Lactate increases also with severe hypoxia even when PCO_2 does not change much. This was demonstrated in an earlier study (2) and again in the present one. Because hypocapnia

by itself does not increase markedly, the ratio of excess lactate increase resulting from hypoxia in combination with hypocapnia shows some order of complementarity in the denominator. In other words, the combination of hypoxia and hypocapnia should affect excess lactate less than the lactate increase alone would make the ratio smaller. The quantity $(\Delta L/\Delta L \times 100)$ for hypocapnic hypoxia was 62.4 ± 18.8 ; for eucapnic hypoxia, 76.5 ± 12.9 ; and for hypercapnic hypoxia, 80.4 ± 18.7 . With hypocapnic hypoxia, therefore, excess lactate accounted for less of the total lactate increase, and this was significant ($P < .05$) in comparison to eucapnic and hypercapnic hypoxia. The ratio did not differ significantly, however, between the latter two conditions.

The extrapolative reasoning by which excess lactate was supposed to represent an intracellular change in the ratio of NAD to NADH (7) is tenuous enough to allow for an equally tenuous explanation of the results illustrated in figures 1 and 2. Intracellular alkalosis may interact with intracellular hypoxia to produce more lactate, even in excess to an increase in pyruvate, for a given level of oxygen deficit. Invocation of an interaction, however, is more descriptive than explanatory. Furthermore, in terms of equilibria between pyruvate, lactate, and the electron transport chain, decreased hydrogen ion concentration might reasonably be expected to depress lactate formation (15). An alternative proposition is that net O_2 deficit or repayment is not always a valid measure of the true energy deficit because the baseline energy demand does not remain unchanged during and after hypoxia. This was suggested before (2) and now will be expounded in more detail.

Reversibility of hemorrhagic shock has been related to the size of O_2 deficit formed by the consequent stagnant hypoxia (3). Nahas et al. (11) showed, however, that hemorrhage, which was not enough to embarrass O_2 transport capacity, actually caused an increase in O_2 uptake of anesthetized dogs. This effect was attributed to the calorigenesis of increased catecholamine release and was found to be

inhibited by hypercapnic acidosis. Additional work by Poyart and Nahas (13) using infusions of catecholamines proved that O_2 uptake was increased 30% and that it was not increased in the presence of hypercapnia. In similar experiments in this laboratory, increases of up to 45% in O_2 uptake have been obtained when norepinephrine was infused.

The pertinence of this kind of experimentation applies to the use of an extrapolated baseline O_2 uptake to measure an O_2 deficit. If hypoxia stimulates the release of catecholamines, then the actual energy deficit that cannot be met by aerobic metabolism may be greater than that based on a control measurement of O_2 uptake. Fowler et al. (6) did find, by bioassay, increased output of "norepinephrine-like" substances in the left adrenal vein of anesthetized dogs made hypoxic. To explain adequately the results presented here, it would be necessary to make the additional hypothesis of a potentiating effect of alkalosis on the calorigenesis. Nahas and Poyart (10) measured even greater increases in O_2 uptake in hyperventilated dogs infused with catecholamines than the increases obtained at normal pH. It would not be correct to call this a potentiating effect, however, because they found that, even in passively hyperventilated dogs, O_2 uptake was increased by hyperventilation alone and that this was additive to the increase caused by catecholamine infusion. Nevertheless, in terms of O_2 uptake, there is a gradation of effect attributable to pH.

It seems reasonable to suppose, then, that baseline energy demand rose considerably during hypocapnic hypoxia, less during eucapnic hypoxia, and not at all or even decreased during hypercapnic hypoxia. This would explain the marked differentiation into three groups evi-

dent in figures 1 and 2. In figure 1, particularly during hypocapnia, there must have been some additional influence of hypocapnia on lactate increase. A measure of this is the greater upward displacement of the hypocapnia line than was seen in figure 2 for excess lactate and in the smaller ratio of XL to ΔL with hypocapnic hypoxia.

The significant tendency for the hypocapnic dogs to overpay the observed O_2 deficit also fits the proposed sequence (fig. 5). A rising baseline during hypoxia could not be seen, but its gradual return to control would be included in recovery measurements. With a relatively gross underestimate of the deficit, therefore, it would appear that the deficit was overpaid by dogs recovering from hypocapnic hypoxia. The results from the other two groups are not as clear in the relation of NOR to NOD. If it is assumed that the least error in estimating the energy deficit was present in hypercapnic hypoxia, then it must follow that the energy deficit incurred during hypoxia is never fully repaid. This may prove to be true, but the proof is not to be found in these results.

Because pH affects lactate metabolism and also affects the calorigenesis associated with increased release of catecholamines, it becomes of some interest to separate these two actions. Nahas and Poyart (10) indicated how this might be done when they compared the inhibitory action of acidosis to that of β -adrenergic blocking compounds. It would be of interest to repeat the experiments reported here using such compounds. As it now stands, however, the results of these experiments offer further evidence of the difficulties encountered when an attempt is made to quantitate the severity of tissue hypoxia.

REFERENCES

1. Bain, J. A., and J. R. Klein. Effect of carbon dioxide on brain glucose, lactate, pyruvate, and phosphates. *Amer. J. Physiol.* 158:478-484 (1949).
2. Cain, S. M. O_2 deficit incurred during hypoxia and its relation to lactate and excess lactate. *Amer. J. Physiol.* 213:57-63 (1967).
3. Crowell, J. W., and E. E. Smith. Oxygen deficit and irreversible hemorrhagic shock. *Amer. J. Physiol.* 206:313-316 (1964).
4. Eichenholz, A. R., R. O. Mulhauser, W. E. Anderson, and F. M. MacDonald. Primary hypocapnia: A cause of metabolic acidosis. *J. Appl. Physiol.* 17:283-288 (1962).

5. Eldridge, F., and J. Salzer. Effect of respiratory alkalosis on blood lactate and pyruvate in humans. *J. Appl. Physiol.* 22:461-468 (1967).
6. Fowler, N. O., R. Shabetan, and J. C. Holmen. Adrenal medullary secretion during hypoxia, bleeding and rapid intravenous infusion. *Circ. Res.* 9:427-435 (1961).
7. Huckabee, W. E. Relationships of pyruvate and lactate during anaerobic metabolism. I. Effects of infusion of pyruvate or glucose and of hyperventilation. *J. Clin. Invest.* 37:244-254 (1958).
8. Katzman, R., C. A. Villet, and H. K. Beech. Effect of increased carbon dioxide concentrations on fixed acid production in vitro. *Amer. J. Physiol.* 172:317-323 (1953).
9. Long, C. N. H. The lactic acid in the blood of a resting man. *J. Physiol. (London)* 58:455-460 (1924).
10. Nahas, G. G., and C. Poyart. Effect of arterial pH alterations on metabolic activity of nor-epinephrine. *Amer. J. Physiol.* 212: 765-772 (1967).
11. Nahas, G. G., L. Triner, H. S. Small, W. M. Mangr, and D. V. Habib. Alterations in O_2 uptake following hemorrhage in dogs. *Amer. J. Physiol.* 210:1009-1014 (1966).
12. Plum, F., and J. B. Posner. Blood and cerebrospinal fluid lactate during hyperventilation. *Amer. J. Physiol.* 212:864-870 (1967).
13. Poyart, C., and G. G. Nahas. Inhibition of catecholamine-induced catechologenesis and lipolysis by hypercapnic acidosis. *Amer. J. Physiol.* 211: 161-168 (1966).
14. Takano, N. Blood lactate accumulation and its causative factor during passive hyperventilation in dogs. *Jap. J. Physiol.* 16:481-496 (1966).
15. Tobin, E. B. In vivo influences of hydrogen ions on lactate and pyruvate in blood. *Amer. J. Physiol.* 207:601-605 (1964).
16. Zborowska-Sluis, D. T., and J. B. Dossator. Hyperlactatemia of hyperventilation. *J. Appl. Physiol.* 22:746-755 (1967).

Unclassified

Security Classification

DOCUMENT CONTROL DATA - R & D

1. SECURITY CLASSIFICATION OF REPORT (If abstract is to be entered when the original report is classified)	
2. ORIGINATING ACTIVITY (If not the same as the reporting activity)	
USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas	
3. SECURITY CLASSIFICATION OF ABSTRACT	
Unclassified	
4. TITLE AND SUBTITLE	
EFFECT OF PCO_2 ON THE RELATION OF LACTATE AND EXCESS LACTATE TO O_2 DEFICIT	
5. AUTHOR (Last name, first name, middle initial, last name)	
Stephen M. Cain	
6. REPORT DATE	7. TOTAL NO. OF PAGES
December 1967	6
8. CONTRACT OR GRANT NO.	9. NO. OF REFS
	16
10. PROJECT NO.	11. ORIGINATOR'S REPORT NUMBER(S)
Task No. 775801	SAM-TR-67-109
12. DISTRIBUTION STATEMENT	
This document has been approved for public release and sale; its distribution is unlimited.	
13. SUPPLEMENTARY NOTES	14. SPONSORING MILITARY ACTIVITY
	USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas
15. ABSTRACT	
<p>When anesthetized dogs were made hypoxic at constant ventilation, increases in arterial lactate (ΔL) compared as well to net O_2 deficit (NOD) as did excess lactate (XL). It was asked whether this would hold true if PCO_2 was varied during hypoxia. Twelve dogs were made hypoxic for 30 minutes while eucapnic ($PCO_2 = 40$ torr) and again while hypercapnic ($PCO_2 = 77$ torr), with appropriate control and recovery periods. Another group of 12 dogs were treated similarly except one hypoxic period was hypocapnic ($PCO_2 = 18$ torr) and the other eucapnic. NOD was estimated from the total decrease in V_{O_2} during hypoxia by assuming that baseline V_{O_2} would have been unchanged if P_{O_2} was not limited, and by estimating the change in O_2 stores during hypoxia. Net O_2 repayment (NOR) was estimated similarly. In a graph of ΔL against NOD, three different lines were obtained according to the PCO_2 level. The same was true for XL against NOD. In 36 of 48 comparisons, NOR was less than NOD. Of the 12 comparisons in which NOR was larger, 7 were hypocapnic, 4 were eucapnic, and only 1 was hypercapnic. In addition to direct effects of altered intracellular pH on lactate metabolism, PCO_2 may also alter baseline energy demand during hypoxia by its effect on calorogenesis of liberated catecholamines.</p>	

DD FORM 1473
1 NOV 65

Unclassified

Security Classification

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Physiology Hypoxia Hypocapnia Hypercapnia Oxygen debt						